Amendments to the Specification

Please replace the paragraph beginning at page 15, line 4 with the following amended paragraph:

Figure 2 shows the sequence alignments of the amino acid sequences of MASP-2 (clone phl-4) (SEQ ID NO:2), MASP-1[17,22] (SEQ ID NO:6), C1r[23,24] (SEQ ID NO:7) and C1s[25,26] (SEQ ID NO:8).

Please replace the paragraph beginning at page 15, line 14 with the following amended paragraph:

Figure 6 shows the cDNA sequence (SEQ ID NO:3) and deduced amino acid (SEQ ID NO:2) sequence of MASP-2.

Please replace the paragraph beginning at page 44, line 24 with the following amended paragraph:

Animals, primed with BCG (Bacillus Calmette Gurin vaccine) were immunized with synthetic peptides coupled to PPD (tuberculin purified protein derivative) according to C. Koch, The State Serum Institute, Copenhagen. Antibody designated anti-N' MASP-1, anti-C' MASP-1 and anti-N' MASP-2 were from rabbits immunized with peptides corresponding to the first 19 amino acid residues of MASP-1 (SEQ ID NO:6), the last 19 amino acid residues of MASP-1 (SEQ ID NO:6) and the first 19 amino acid residues of MASP-2 (SEQ ID NO:2), respectively. Chicken anti-C' MASP-2 antibody was from chickens immunized with a mixture of two peptides representing sequences in the C-terminal part of MASP-2 (residues 505 to 523 and 538 to 556). All peptides had an additional C-terminal cysteine for coupling. Antibody and normal chicken IgG was purified from yolk[26]. Monoclonal anti-MBL antibody, IgG_1-kappa (clone 131-1) and control IgG_1-kappa (clone MOPC 21) were purified by Protein A affinity chromatography. $F(ab')_2$ rabbit anti-human C4 and $F(ab')_2$ rabbit anti-human C1q were produced by pepsin digestion of rabbit anti-human C4 and rabbit anti-human C1q (DAKO, Glostrup, Denmark). For staining of Western blots antibodies were used at 1µg/ml. Bound chicken antibody was visualized with rabbit anti-chicken IgG followed by

peroxidase-labelled goat anti-rabbit IgG and development using the enhanced chemiluminescence technique. Bound mouse and rabbit antibodies were visualized with peroxidaselabelled rabbit anti-mouse IgG and peroxidase-labelled goat anti-rabbit IgG, respectively.

Please replace the paragraph beginning at page 46, line 10 with the following amended paragraph:

The liver is the primary site of synthesis of C1r, C1s, and MASP-1. Thus, RNA from liver was used as template for RT-PCR with primers deduced from the obtained peptide sequences. First strand synthesis of cDNA was carried out with 1.3 µg human liver RNA using a First-Strand cDNA Synthesis Kit (Pharmacia). PCR was performed on this cDNA using degenerate sense and antisense primers derived from the amino acid sequences EYANDQER (SEQ ID NO:4) and KPFTGFEA (SEQ ID NO:5), respectively. The PCR program consisted of 1 cycle with annealing at 50°C.; 1 cycle with annealing at 55°C., and 33 cycles with annealing at 60°C. The resulting 300 bp PCR product was cloned into the *E. coli* plasmid PCRII using the TA-cloning kit (InVitrogen) and the nucleotide sequence of the insert was determined.

Please replace the paragraph beginning at page 46, line 24 with the following amended paragraph:

The nucleotide sequence of the resulting 300 bp RT-PCR product contained an open reading frame (ORF) with a deduced amino acid sequence confirming the sequences of the peptides from which the primers were derived as well as that of another of the sequenced peptides. The insert of this plasmid was radioactivly labelled and used as a probe for screening a total of 8 X 10^5 clones in a commercial human liver library (Stratagene). Sixteen clones hybridized and the 4 longest (phl-1,2,3 and 4) were completely sequenced. Sequence analysis revealed that all four clones represent reverse transcripts of the same novel human mRNA species. The longest clone, phl-4, comprises 2475 bp starting

with a 5' untranslated region of 36 bp followed by an ORF of 2061 bp and a 3' untranslated region of 378 bp ending with a poly-A tail. The nucleotide sequence (SEQ ID NO:3) of phl-4 is shown in FIG. 6 together with the translated amino acid sequence (SEQ ID NO:2). The sequences are deposited at the EMBL nucleotide sequence data base (accession no. Y09926). While the sequence of phl-1 and -2 were in total agreement with phl-4, the nucleotide sequence of phl-3 differs from phl-4 at two positions, a transversion at nucleotide position 1147 (G to T) and a transition at position 1515 (C to T). The first change leads to the replacement of Asp 356 with Tyr. Because all clones were isolated from a liver library transcribed from RNA isolated from a single donor, the observed difference may represent a polymorphism in the MASP-2 gene, or is due to an error created during construction of the library.

Please replace the paragraph beginning at page 47, line 21 with the following amended paragraph:

The amino acid sequences of the NH_2-terminus as well as all sequenced peptides were identified in the sequence deduced from clone phl-4. The ORF encodes a polypeptide chain of 686 amino acids (SEQ ID NO:2) including a signal peptide of 15 residues. Omitting the signal peptide, the calculated M_r is 74,153, in agreement with the 76 kDa observed on SDS-PAGE (Fig. 1), the isoelectric point is 5.43 and the molar extinction coefficient is 113,640 (i.e. OD_{280nm}=1.54 at 1 mg/ml). In contrast to MASP-1 (SEQ ID NO:6) the sequence contains no sites for N-linked glycosylation. The three amino acid residues which are essential for the active centre in serine proteases (His 468, Asp 517, and Ser 618) are present.

Please replace the paragraph beginning at page 48, line 2 with the following amended paragraph:

The amino acid sequence deduced from the cDNA sequences is homologous to those of MASP-1 (SEQ ID NO:6), C1r (SEQ ID NO:7)

and C1s (SEQ ID NO:8) (FIG. 2). Notably, the domain organization is common to these four proteins, featuring one C1r/C1s-like domain, one epidermal growth factor-like (EGF-like) domain, followed by a second C1r/C1s-like domain, two complement control protein (CCP) domains, and a serine protease domain. The key residues involved in the calcium-binding motif in the epidermal growth factor-like domains are present in the obtained sequence (SEQ ID NO:2), as well as in MASP-1 (SEQ ID NO:6), C1r (SEQ ID NO:7) and C1s (SEQ ID NO:8). In addition, the substrate specificity related residue, 6 residues before the active site serine, is aspartic acid in all four proteins. MASP-1, C1r, and C1s are all activated by cleavage of the peptide bond between the residues Arg and Ile located between the second CCP domain and the serine protease domain. The resulting polypeptide chains (the largest referred to as the "heavy chain" and the smallest as "light chain") are held together by a disulphide bond. By analogy, our results indicate that the 52 kDa polypeptide, recognized by antibody against the N-terminal of MASP-2 after SDS-PAGE under reducing conditions, is the heavy chain of MASP-2, whereas the 31 kDa polypeptide, recognized by antibody against the C-terminal of MASP-2, is the light chain. As seen in Fig. 2, Arg and Ile are present in MASP-2 (SEQ ID NO:2) at the expected positions between the second CCP domain and the protease domain.

Please replace the paragraph at page 48, line 28 with the following amended paragraph:

Identities and similarities between the four proteins were studied based on the alignment in Fig. 2. A bias of 6 was added to each term of the mutation data matrix (250 PAMS) and a break penalty of 6 was used. Identical residues in all four species are indicated by asterisks. The beginning of the C1r/C1s-like domains, the EGF-like domain and the CCP domains are indicated above the sequences. The aligned cysteines are shaded. The potential cleavage site between Arg and Ile residues, which

generates heavy and light chains, is identical to the site where the serine protease domain starts. The three amino acid residues, which are essential for the active centre in serine proteases (His 468, Asp 517 and Ser 618), are indicated (◊). The cysteines in the histidine-loop of MASP-1 (SEQ ID NO:6) are marked (∇). The sequences obtained by amino acid sequencing of peptides are underlined. The identities between the proteins (Fig. 2) are all in the range of 39% to 45% and gives no clue to functional relatedness. The similarity, i.e. taking into account residues of similar nature as well as identical residues, between the proteins (Fig. 3b) are between 39 and 52% with the least similarity being between MASP-1 (SEQ ID NO:6) and C1s (SEQ ID NO:8) (39%) and the highest similarity between MASP-1 (SEQ ID NO:6) and C1r (SEQ ID NO:7) (52%) and between MASP-1 (SEQ ID NO:6) and MASP-2 (SEQ ID NO:2) (52%). MASP-2 (SEQ ID NO:2) shows similarity with C1r (46%) (SEQ ID NO:7) and C1s (47%) (SEQ ID NO:8). Whereas the relative identities gives no clue as to functional relatedness the similarity score between C1s and MASP-2 is significantly higher than between C1s and MASP-1 while MASP-1 is more similar to C1r than to C1s, suggesting that MASP-2, like C1s, could be a C2 and C4 cleaving enzyme. Several features of the sequences suggest that MASP-2, C1r and C1s have evolved by gene duplication and divergence from a MASP-1 ancestor. Only the MASP-1 (SEQ ID NO:6) sequence contains the histidine loop, characteristic of trypsin-like serine proteases[27]. The active site serine is encoded by a TCN codon (N is A, T, G or C) in MASP-1 as in most serine proteases, whereas in MASP-2 (SEQ ID NO:2), C1r (SEQ ID NO:7) and C1s (SEQ ID NO:8) it is encoded by an AGY codon (where Y is T or C). In most serine proteases, including MASP-1 (SEQ ID NO:6), a proline residue is found at the third position downstream from the active site serine, whereas a different amino acid is found in MASP-2 (SEQ ID NO:2), C1s (SEQ ID NO:8) and C1r (SEQ ID NO:7) (alanine in MASP-2 and C1s, valine in C1r). Based on these analogies one may predict that the catalytic domain of MASP-2 is encoded by a

single exon as in C1r and C1s, whereas most other serine proteases, including MASP-1[28] (SEQ ID NO:6), have split exons.